

**PATENT**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

**In re Application of:**

Havenga et al.

**Serial No.:** To be assigned

**Filed:** November 13, 2001

**For:** GENE DELIVERY VECTORS WITH  
CELL TYPE SPECIFICITY FOR  
MESENCHYMAL STEM CELLS

**Examiner:** To be assigned

**Group Art Unit:** To be assigned

**Attorney Docket No.:** 5006.1US

**NOTICE OF EXPRESS MAILING**

Express Mail Mailing Label Number: EL 740547505 US

Date of Deposit with USPS: November 13, 2001

Person making Deposit: Orlena Howell

**Preliminary Amendment**

Commissioner for Patents  
Washington, D.C. 20231

Sir:

Before examination of the application and calculation of the filing fees, please amend the  
above identified patent application as follows:

IN THE CLAIMS:

Applicants would note that all of the pending claims, not just the amended ones, are set forth in the following section for the convenience of the Office.

1. A nucleic acid delivery vehicle having at least a tissue tropism for mesenchymal stem cells.
2. The nucleic acid delivery vehicle of claim 1, further having at least partially reduced tissue tropism for liver cells.
3. (Amended) The nucleic acid delivery vehicle of claim 2, wherein said tissue tropism is provided by at least a part of a virus capsid or a functional derivative and/or analogue thereof.
4. The nucleic acid delivery vehicle of claim 3, wherein said virus capsid comprises proteins, or functional parts, derivatives and/or analogues thereof, from at least two different viruses.
5. The nucleic acid delivery vehicle of claim 4, wherein at least one of said at least two different viruses is an adenovirus.
6. (Amended) The nucleic acid delivery vehicle of claim 4, wherein at least one of said at least two different viruses is an adenovirus of subgroup B.
7. (Amended) The nucleic acid delivery vehicle of claim 4, wherein at least one of said proteins comprises a tissue tropism determining part of a fiber protein derived from a subgroup B adenovirus a functional derivative and/or analogue thereof.
8. (Amended) The nucleic acid delivery vehicle of claim 6, wherein said subgroup B adenovirus is adenovirus 16.

9. (Amended) The nucleic acid delivery vehicle of claim 6, further comprising at least one protein derived from an adenovirus not belonging to subgroup B, or a functional part, derivative and/or analogue thereof.
10. The nucleic acid delivery vehicle of claim 9, wherein said at least one protein or a functional part, derivative and/or analogue thereof not derived from an adenovirus of subgroup B is derived from an adenovirus of subgroup C.
11. (Amended) The nucleic acid delivery vehicle of claim 3, further comprising adenoviral nucleic acid.
12. (Amended) The nucleic acid delivery vehicle of claim 3, comprising adenoviral nucleic acid from at least two different adenoviruses.
13. (Amended) The nucleic acid delivery vehicle of claim 11, wherein said adenoviral nucleic acid at least encodes a fiber protein comprising at least a tissue tropism determining part of a subgroup B adenovirus fiber protein or a functional derivative and/or analogue thereof.
14. (Amended) The nucleic acid delivery vehicle of claim 11, wherein said adenoviral nucleic acid is a modified nucleic acid such that the capacity of said adenoviral nucleic acid to replicate in a target cell has been reduced or disabled.
15. (Amended) The nucleic acid delivery vehicle of claim 12, wherein said adenoviral nucleic acid is a modified nucleic acid such that the capacity of a host immune system to mount an immune response against adenovirus proteins encoded by said adenoviral nucleic acid has been diminished.

16. (Amended) The nucleic acid delivery vehicle of claim 3 further comprising a minimal adenovirus vector or an Ad/AAV chimeric vector.

17. (Amended) The nucleic acid delivery vehicle of claim 3 further comprising at least one nucleic acid of interest.

18. (Amended) The nucleic acid delivery vehicle of claim 3, wherein said nucleic acid delivery vehicle is a subgroup B adenovirus capsid comprising at least one nucleic acid of interest.

19. The nucleic acid delivery vehicle of claim 18, wherein said at least one nucleic acid of interest further comprises at least one subgroup B adenovirus nucleic acid.

20. The nucleic acid delivery vehicle of claim 19, wherein said at least one subgroup B adenovirus nucleic acid has been deprived of the capacity to express E1-region encoded proteins.

21. (Amended) The nucleic acid delivery vehicle of claim 18, wherein said subgroup B adenovirus capsid is derived from adenovirus 16.

22. (Amended) A process for producing the nucleic acid delivery vehicle of claim 3, said method comprising:

providing a cell with means for the assembly of said nucleic acid delivery vehicle wherein said means includes a means for the production of an adenovirus fiber protein, wherein said adenovirus fiber protein comprises at least a tissue tropism determining part of a subgroup B adenovirus or a functional derivative and/or analogue thereof.

23. (Amended) A cell for the production of the nucleic acid delivery vehicle of claim 3, said cell comprising:

means for the assembly of said nucleic acid delivery vehicle wherein said means includes a means for the production of an adenovirus fiber protein, wherein said adenovirus fiber protein comprises at least a tissue tropism determining part of a subgroup B adenovirus fiber protein.

24. (Amended) A pharmaceutical preparation comprising the nucleic acid delivery vehicle of claim 1.

25. A method for the treatment of a disease that is treatable by transfer of a nucleic acid encoding a therapeutic proteinaceous molecule or RNA to mesenchymal stem cells comprising administering the pharmaceutical preparation of claim 24.

26. (Amended) A method for the delivery of nucleic acid to mesenchymal stem cells comprising administering the nucleic acid delivery vehicle of claim 1.

27. (Amended) A method for the generation of a nucleic acid library comprising analyzing the nucleic acid delivery vehicle of claim 1.

28. A method for the delivery of nucleic acid to a mesenchymal stem cell comprising administering the nucleic acid delivery vehicle of claim 1, wherein said nucleic acid delivery vehicle comprises a fiber protein of adenovirus 16 or a functional part, derivative and/or analogue thereof.

29. (Amended) A pharmaceutical preparation for the treatment of rheumatoid arthritis comprising the nucleic acid delivery vehicle of claim 1.

30. The pharmaceutical preparation of claim 29, wherein said nucleic acid delivery vehicle comprises a gene encoding IL-10 or a functional equivalent thereof.

31. (Amended) A method for tissue engineering comprising administering the nucleic acid delivery vehicle of claim 1.

32. (Amended) A pharmaceutical preparation for providing bone regeneration comprising the nucleic acid delivery vehicle of claim 1.

33. (Amended) A pharmaceutical preparation for providing bone regeneration comprising a mesenchymal stem cell provided with a gene of interest through the nucleic acid delivery vehicle of claim 1.

34. (Amended) The pharmaceutical preparation of claim 32 wherein said nucleic acid delivery vehicle is provided with a gene encoding bone morphogenesis protein-2 and/or LIM mineralization protein-1 or a functional equivalent of either.

35. (Amended) A pharmaceutical preparation for the treatment of multiple sclerosis comprising a mesenchymal stem cell provided with a gene of interest through the nucleic acid delivery vehicle of claim 1.

36. (Amended) A pharmaceutical preparation for promoting angiogenesis comprising a mesenchymal stem cell provided with a gene of interest through the nucleic acid delivery vehicle of claim 1.

37. (Amended) A mesenchymal stem cell comprising a nucleic acid delivered to said mesenchymal stem cell through the nucleic acid delivery vehicle of claim 1.



46. The cell of claim 23, wherein said cell is or is derived from a PER.C6 cell.
47. A method for the generation of a nucleic acid library comprising analyzing the cell of claim 23.



### Remarks

The application is to be amended without prejudice or disclaimer as previously set forth, which should not be viewed as narrowing or limiting the claims. The amendments are sought to conform the application to a form more consistent with Office practice by removing multiple dependencies. It is respectfully submitted that no new matter has been added by the amendments. Should the Office determine that additional issues remain, which might be resolved by a telephone conference, it is respectfully invited to contact applicants' undersigned attorney.

Respectfully Submitted,



Allen C. Turner

Registration Number 33,041

Attorney for Applicants

TRASKBRITT, PC

P.O. Box 2550

Salt Lake City, Utah 84110

Telephone: (801) 532-1922

Date: November 6, 2001

Enclosure: Version With Markings to Show Changes Made

VERSION WITH MARKINGS TO SHOW CHANGES MADE

3. (Amended) The nucleic acid delivery vehicle of [claim 1 or] claim 2, wherein said tissue tropism is provided by at least a part of a virus capsid or a functional derivative and/or analogue thereof.
6. (Amended) The nucleic acid delivery vehicle of claim 4 [or claim 5], wherein at least one of said at least two different viruses is an adenovirus of subgroup B.
7. (Amended) The nucleic acid delivery vehicle of claim 4, [claim 5, or claim 6,] wherein at least one of said proteins comprises a tissue tropism determining part of a fiber protein derived from a subgroup B adenovirus a functional derivative and/or analogue thereof.
8. (Amended) The nucleic acid delivery vehicle of claim 6 [or claim 7], wherein said subgroup B adenovirus is adenovirus 16.
9. (Amended) The nucleic acid delivery vehicle of claim 6, [claim 7, or claim 8,] further comprising at least one protein derived from an adenovirus not belonging to subgroup B, or a functional part, derivative and/or analogue thereof.
11. (Amended) The nucleic acid delivery vehicle of [any one of claims 1 through 10]claim 3, further comprising adenoviral nucleic acid.
12. (Amended) The nucleic acid delivery vehicle of [any one of claims 1 through 11]claim 3, comprising adenoviral nucleic acid from at least two different adenoviruses.

13. (Amended) The nucleic acid delivery vehicle of claim 11 [or claim 12], wherein said adenoviral nucleic acid at least encodes a fiber protein comprising at least a tissue tropism determining part of a subgroup B adenovirus fiber protein or a functional derivative and/or analogue thereof.

14. (Amended) The nucleic acid delivery vehicle of claim 11, [claim 12 or claim 13,] wherein said adenoviral nucleic acid is a modified nucleic acid such that the capacity of said adenoviral nucleic acid to replicate in a target cell has been reduced or disabled.

15. (Amended) The nucleic acid delivery vehicle of [any one of claims 11 through 14]claim 12, wherein said adenoviral nucleic acid is a modified nucleic acid such that the capacity of a host immune system to mount an immune response against adenovirus proteins encoded by said adenoviral nucleic acid has been diminished.

16. (Amended) The nucleic acid delivery vehicle of [any one of claims 1 through 15,]claim 3 further comprising a minimal adenovirus vector or an Ad/AAV chimeric vector.

17. (Amended) The nucleic acid delivery vehicle of [any one of claims 1 through 16,]claim 3 further comprising at least one nucleic acid of interest.

18. (Amended) The nucleic acid delivery vehicle of [any one of claims 1 through 17]claim 3, wherein said nucleic acid delivery vehicle is a subgroup B adenovirus capsid comprising at least one nucleic acid of interest.

21. (Amended) The nucleic acid delivery vehicle of claim 18, [claim 19, or claim 20,] wherein said subgroup B adenovirus capsid is derived from adenovirus 16.

22. (Amended) A process for producing the nucleic acid delivery vehicle of [any one of claims 1 through 21]claim 3, said method comprising:

providing a cell with means for the assembly of said nucleic acid delivery vehicle wherein said means includes a means for the production of an adenovirus fiber protein, wherein said adenovirus fiber protein comprises at least a tissue tropism determining part of a subgroup B adenovirus or a functional derivative and/or analogue thereof.

23. (Amended) A cell for the production of the nucleic acid delivery vehicle of [any one of claims 1 through 21]claim 3, said cell comprising:

means for the assembly of said nucleic acid delivery vehicle wherein said means includes a means for the production of an adenovirus fiber protein, wherein said adenovirus fiber protein comprises at least a tissue tropism determining part of a subgroup B adenovirus fiber protein.

24. (Amended) A pharmaceutical preparation comprising the nucleic acid delivery vehicle of [any one of claims 1 to 21]claim 1.

26. (Amended) A method for the delivery of nucleic acid to mesenchymal stem cells comprising administering the nucleic acid delivery vehicle of [any one of claims 1 to 22]claim 1.

27. (Amended) A method for the generation of a nucleic acid library comprising analyzing the nucleic acid delivery vehicle of [any one of claims 1 to 21]claim 1.

29. (Amended) A pharmaceutical preparation for the treatment of rheumatoid arthritis comprising the nucleic acid delivery vehicle of [any one of claims 1 to 21]claim 1.

31. (Amended) A method for tissue engineering comprising administering the nucleic acid delivery vehicle of [any one of claims 1 to 22]claim 1.

32. (Amended) A pharmaceutical preparation for providing bone regeneration comprising the nucleic acid delivery vehicle of [any one of claims 1 to 22]claim 1.

33. (Amended) A pharmaceutical preparation for providing bone regeneration comprising a mesenchymal stem cell provided with a gene of interest through the nucleic acid delivery vehicle of [any one of claims 1 to 22]claim 1.

34. (Amended) The pharmaceutical preparation of claim 32 [or claim 33] wherein said nucleic acid delivery vehicle is provided with a gene encoding bone morphogenesis protein-2 and/or LIM mineralization protein-1 or a functional equivalent of either.

35. (Amended) A pharmaceutical preparation for the treatment of multiple sclerosis comprising a mesenchymal stem cell provided with a gene of interest through the nucleic acid delivery vehicle of [any one of claims 1-22]claim 1.

36. (Amended) A pharmaceutical preparation for promoting angiogenesis comprising a mesenchymal stem cell provided with a gene of interest through the nucleic acid delivery vehicle of [any one of claims 1-22]claim 1.

37. (Amended) A mesenchymal stem cell comprising a nucleic acid delivered to said mesenchymal stem cell through the nucleic acid delivery vehicle of [any one of claims 1-21]claim 1.